CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER
21-379

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

Review for HFD-580

July 18, 2002

NDA:	**21-379-AZ**
Drug Product Name	
Proprietary:	Eligard 22.5 (LA-2550) mg
Non-proprietary:	Leuprolide Acetate for Injectable Suspension
Drug Product Classification:	3S GnRH agonist
Review Number:	2
Subject of this Review	
Submission Date:	June 26, 2002
Receipt Date:	June 27, 2002
Consult Date:	June 27, 2002
Date Assigned for Review:	July 18, 2002
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	September 25, 2001 (NDA 21-379) April 25, 2002 (NDA 21-379-BZ)
Date(s) of Previous Micro Review(s):	May 15, 2002 (NDA 21-379) May 18, 2002 (NDA 21-379-BZ)
Applicant/Sponsor	
Name:	Atrix Laboratories Inc.
Address:	2579 Midpoint Dr. Fort Collins, CO 80525-4417
Representative:	Johanna Matz
Telephone:	(970) 482-5868
Name of Reviewer:	Stephen E. Langille, Ph.D.
Conclusion:	Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** N/A

2. **SUPPLEMENT PROVIDES FOR:** N/A

3. **MANUFACTURING SITE:** /

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**

- Subcutaneous Injection
- 22.5 mg

5. **METHOD(S) OF STERILIZATION:** —

6. **PHARMACOLOGICAL CATEGORY:** Palliative treatment for prostrate cancer.

B. **SUPPORTING/RELATED DOCUMENTS:**
The first review of NDA 21-379 was completed on May 10, 2002. The response to deficiencies listed in the review were provided on June 26, 2002.

C. **REMARKS:** The drug product is packaged in two separate syringes. Syringe A contains ARTIGEL and is — sterilized using — Syringe B contains leuprolide acetate and is — The contents of the two syringes are mixed together prior to administration.

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Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 21-379 is recommended for approval from the standpoint of microbial product quality.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -

The drug product is packaged in two separate syringes and mixed prior to injection. Syringe A contains the ATRIGEL delivery system and syringe B contains lyophilized leuprolide acetate. Syringe B and its contents are [redacted] sterilized using [redacted] [redacted] Leuprolide acetate is [redacted] dispensed into syringe B.

B. Brief Description of Microbiology Deficiencies -
No deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies -

III. Administrative

A. Reviewer's Signature /S/ _____

B. Endorsement Block
In DFS /S/

C. CC Block
In DFS

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/s/

Stephen Langille
7/22/02 09:39:47 AM
MICROBIOLOGIST

Peter Cooney
7/22/02 02:24:06 PM
MICROBIOLOGIST

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Product Quality Microbiology Review
Review for HFD-580
10 May 2002

NDA:	**21-379**
Drug Product Name	
Proprietary:	Eligard 22.5 (LA-2550) mg
Non-proprietary:	Leuprolide Acetate for Injectable Suspension
Drug Product Classification:	3S GnRH agonist
Review Number:	1
Subject of this Review	
Submission Date:	September 25, 2001
Receipt Date:	October 5, 2001
Consult Date:	October 30, 2001
Date Assigned for Review:	December 18, 2001
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	N/A
Date(s) of Previous Micro Review(s):	N/A
Applicant/Sponsor	
Name:	Atrix Laboratories Inc.
Address:	2579 Midpoint Dr. Fort Collins, CO 80525-4417
Representative:	Elyse Wolff
Telephone:	(970) 482-5868
Name of Reviewer:	Stephen E. Langille, Ph.D.
Conclusion:	Approvable pending resolution of microbiology deficiencies.

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** N/A

2. **SUPPLEMENT PROVIDES FOR:** N/A

3. **MANUFACTURING SITE:**

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**

- Subcutaneous Injection
- 22.5 mg

5. **METHOD(S) OF STERILIZATION:**

6. **PHARMACOLOGICAL CATEGORY:** Palliative treatment for prostrate cancer.

B. **SUPPORTING/RELATED DOCUMENTS:**
NDA 21-379 amendment #3 was submitted on March 19, 2002 to address microbiology issues raised in the review of a related drug product, Eligard™ 7.5 mg.

C. **REMARKS:** The drug product is packaged in two separate syringes. Syringe A contains ARTIGEL and is sterilized using . Syringe B contains leuprolide acetate and is . The contents of the two syringes are mixed together prior to administration.

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Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 21-379 is approvable pending the resolution of microbiology deficiencies.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -

The drug product is packaged in two separate syringes and mixed prior to injection. Syringe A contains the ATRIGEL delivery system and syringe B contains lyophilized leuprolide acetate. Syringe B and its contents are — sterilized using — — . Leuprolide acetate is — dispensed into syringe B.

B. Brief Description of Microbiology Deficiencies -

The Applicant needs to provide:

1. Additional dose mapping information for — sterilization.
2. A better description of the manufacturing facility.
3. Sterilization validation data for the manufacturing equipment.
4. Additional data regarding media fills.
5. Clarification of the integrity testing methods for syringe A.
6. A commitment for sterility testing of syringe A upon release.

C. Assessment of Risk Due to Microbiology Deficiencies -

Adequate sterilization validation data must be provided to insure the sterility of the final drug product. Proper integrity testing and sterility testing are necessary to monitor product quality at release and throughout the shelf-life of the product.

/S/

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
In DFS /S/

C. CC Block
In DFS

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/s/

Stephen Langille
5/16/02 07:16:33 AM
MICROBIOLOGIST

Peter Cooney
5/16/02 09:38:23 AM
MICROBIOLOGIST

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NDA 21-379
Eligard™ 22.5 mg (leuprolide acetate for injectable suspension)

Methods Validation

This will be requested upon approval.

CMR 7/01/02

NDA 21-379
Eligard™ 22.5 mg (leuprolide acetate for injectable suspension)

DSI Memo (GLP Inspection)

aur 7/01/02

No GLP inspection requested.

NDA 21-379
Eligard™ 22.5 mg (leuprolide acetate for injectable suspension)

Statistical Review (Carci Studies)

AR 7/01/02

No review required.